

# EXHIBIT 2

REPRODUCTION OF EXAMPLE 15 OF U.S. PATENT 4,540,602

PART 1R

Into a nominal 400 cc PYREX glass beaker with the following dimensions:

Inside Diameter = 2.75 inch

Vessel Height = 4.25 inch

were added:

32 grams of acetophenetidin (supplied by Sigma Chemical Co., Product Number A2500, "powder" form),

8 grams of hydroxypropyl methylcellulose (purchased from Etsu Chemical Co. as PHARMCOAT, Grade 606), and

200 grams high purity water.

Then, 200 grams of unleaded glass beads were added to the glass vessel. These beads were purchased from Jaygo, Inc., and consisted of a mixture of equal volumetric

quantities of 2, 3, 4 and 5 mm glass beads. The beads were conditioned and cleaned by rolling with water for two hours and drying in room air.

A stainless steel agitator of the same proportions described in Example 15 of U.S. Patent 4,540,602 was fabricated from 316 stainless steel with the following dimensions:

disc diameter	1.975 inches (5 cm)
disc thickness	0.118 inches (3 mm)
shaft diameter	0.118 inches (3 mm)

The shaft was attached concentrically to the upper surface of the disc and was rotated at 400 RPM. The agitator disk was positioned concentrically 3 cm above the bottom of the vessel during the milling process. The composition described above was milled for 90 minutes at 400 RPM. After milling, the dispersion was discharged through a 1 mm wire mesh screen and slurry samples were taken for analytical characterization. Particle size of the dispersion was evaluated using scanning electron micrographs and a low angle light scattering particle sizer made by Microtrac, Inc. (known as the FRA Particle Size Analyzer). The particle size was measured in duplicate and the average of both determinations was as follows:

Volume average diameter:	37.02 microns
Surface average diameter:	15.17 microns

The size of the particles in the unmilled slurry, i.e., the size of the starting material before grinding was as follows:

Volume average diameter:	74.32 microns
Surface average diameter:	47.77 microns

Scanning electron micrographs of the dispersions support the above data.

VARIATIONS OF EXAMPLE 15 OF U.S. PATENT 4,540,602

PART 4R

The procedure described above in Part 1R was repeated except that the milling speed was increased to 1375 RPM and the milling time was increased to 180 minutes. the particle size measured was as follows:

Volume average diameter:	3.49 microns
Surface average diameter:	1.67 microns

PART 2

The procedure described above in part 1R was repeated except that the acetophenetidin was the "crystal" form supplied by Sigma Chemical Co., Product Number A 2375, and 280 gms of grinding media were used. The particle size measured from scanning electron micrographs of the dispersions ranged from about 1 to 10 microns.

The size of the particles in the unmilled slurry, i.e., the starting material before grinding, measured from scanning electron micrographs ranged from about 50 to 1,000 microns.

PART 2A

The procedure described in part 2 above was repeated except that the milling speed was increased to 1375 RPM. The particle size measured from scanning electron micrographs of the dispersion ranged from about 1 to 15 microns.

REPRODUCTION OF EXAMPLE 18 OF U.S. PATENT 4,540,602

PART 3

Into a nominal quart glass jar with the following dimensions:

Inside diameter	=	3.4375 inches
Vessel diameter	=	6.875 inches

were added:

30 grams of hydrocortisone 21-acetate (supplied by Sigma Chemical Co., Product # H4126),  
10 grams of ethylene oxide-propylene oxide copolymer (Pluronic F68, supplied by BASF Corp.),  
100 grams of high purity water, and  
50 grams of ethyl alcohol (100%).

A high speed disperser (Ultra Turrax type TFX # 0473 manufactured by Janke & Kunkel GmbH & Co. KG of the Federal Republic of Germany) was used to process the above blend of ingredients. This device was used to simulate the Politron disperser used in Example 18 of U.S. Patent 4,540,602. The disperser was equipped with the following stator and rotor configuration:

Rotor, model SD-45 (diameter = 1.768 inches)  
Stator Generator G-450 (diameter = 1.7617 inches)

The above ingredients were milled for 30 minutes. During the milling cycle enough heat was generated to evaporate nearly all of the ethanol. This was determined by weighing the contents of the vessel after the milling cycle. Samples of the dispersion were measured using the FRA Particle Size Analyzer. The particle size measured was as follows:

Volume average diameter = 4.51 microns  
Surface average diameter = 2.42 microns

Scanning electron micrographs of these dispersions support the above data.

The size of the particles in the unmilled slurry, i.e., the starting material before grinding measured from scanning electron micrographs ranged from about 0.4 to 10 microns.

VARIATION OF EXAMPLE 18 OF U.S. PATENT 4,540,602

PART 3A

The procedure described in Part 3 above was repeated except that during the milling cycle an additional 100 grams of ethanol were added and the vessel was water jacketed and milled for 30 additional minutes. The particle size measured was as follows:

Volume average diameter = 4.39 microns

Surface average diameter = 2.42 microns

Scanning electron micrographs of this dispersion support the above data.

# HORIBA LA-910

for Windows(TM) Ver.1.20

Dec/04/'96 16:28

Laser scattering particle size distribution analyzer

## PARTICLE SIZE MEASUREMENT DATA

ID# : 961202-771 14:05 Material :  
 Filename : mr1202\_x Source :  
 Sample : Lot Number :

Condition : T%(He-Ne): 98.8% Dist.Form: Std. Sampling times : 15  
 (LAMP): 95.5% R.R.Index 1.19-0.001 (

Agitation : 2 Circultrn : 2 U.sonic : ON( 1)

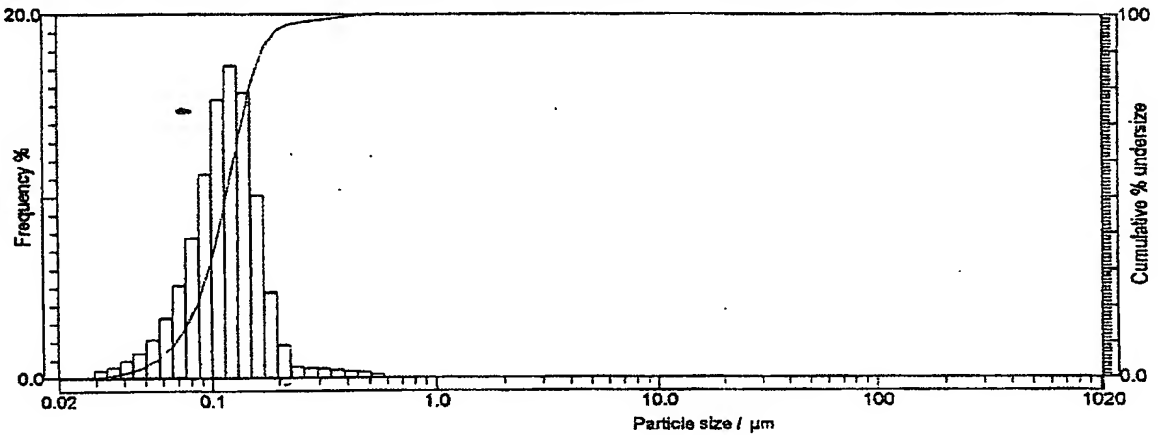
Format : Dist.base : Volume Scaling : Auto Axis : LogX - LinearY

### Data

Median : 0.117µm SP.Area: 572520cm²/cm³ S.D. : 0.054µm  
 Mode : 0.123µm Mean : 0.123µm  
 C.V. : 44.41%

Span : (D 10.0-D 90.0) / D50 = 0.870

Dia. on %( 90.0%) :	0.170µm	% on Dia.( 0.400µm) :	99.2%
Dia. on %( 50.0%) :	0.117µm	% on Dia.( 0.300µm) :	98.3%
Dia. on %( 95.0%) :	0.195µm	% on Dia.( 0.200µm) :	95.6%
Dia. on %( 80.0%) :	0.149µm	% on Dia.( 0.100µm) :	32.6%
Dia. on %( 70.0%) :	0.137µm	% on Dia.( 1.000µm) :	100.0%



Size(µm)	Freq(%)	Und(%)	Size(µm)	Freq(%)	Und(%)	Size(µm)	Freq(%)	Und(%)
1019.5	0.00	100.00	26.11	0.00	100.00	0.669	0.00	100.00
890.1	0.00	100.00	22.80	0.00	100.00	0.584	0.17	100.00
777.1	0.00	100.00	19.90	0.00	100.00	0.510	0.29	99.83
678.5	0.00	100.00	17.38	0.00	100.00	0.445	0.37	99.54
592.4	0.00	100.00	15.17	0.00	100.00	0.389	0.43	99.17
517.2	0.00	100.00	13.25	0.00	100.00	0.339	0.50	98.74
451.6	0.00	100.00	11.56	0.00	100.00	0.296	0.50	98.24
394.2	0.00	100.00	10.10	0.00	100.00	0.259	0.60	97.74
344.2	0.00	100.00	8.816	0.00	100.00	0.226	1.77	97.14
300.5	0.00	100.00	7.697	0.00	100.00	0.197	4.67	95.37
262.4	0.00	100.00	6.720	0.00	100.00	0.172	10.02	90.70
229.1	0.00	100.00	5.867	0.00	100.00	0.150	15.69	80.68
200.0	0.00	100.00	5.122	0.00	100.00	0.131	17.15	64.99
174.6	0.00	100.00	4.472	0.00	100.00	0.115	15.29	47.84
152.5	0.00	100.00	3.905	0.00	100.00	0.100	11.21	32.55
133.1	0.00	100.00	3.409	0.00	100.00	0.087	7.70	21.34
116.2	0.00	100.00	2.976	0.00	100.00	0.076	5.08	13.64
101.5	0.00	100.00	2.599	0.00	100.00	0.067	3.27	8.56
88.58	0.00	100.00	2.269	0.00	100.00	0.058	2.09	5.29
77.34	0.00	100.00	1.981	0.00	100.00	0.051	1.34	3.19
67.52	0.00	100.00	1.729	0.00	100.00	0.044	0.91	1.85
58.95	0.00	100.00	1.510	0.00	100.00	0.039	0.57	0.94
51.47	0.00	100.00	1.318	0.00	100.00	0.034	0.38	0.38
44.94	0.00	100.00	1.151	0.00	100.00	0.029	0.00	0.00
39.23	0.00	100.00	1.005	0.00	100.00	0.026	0.00	0.00
34.25	0.00	100.00	0.877	0.00	100.00	0.022	0.00	0.00
29.91	0.00	100.00	0.766	0.00	100.00			

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Condition :  
 T%(He-Ne): 98.8% Dist.Form: Std. Sampling times : 15  
 (LAMP): 95.5% R.R.Index 1.19-0.001 ( )

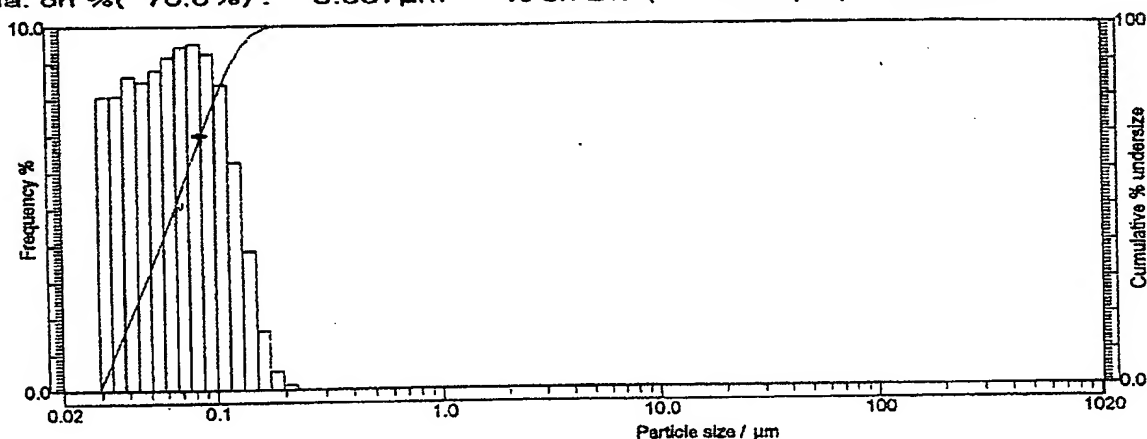
Agitation : 2 Circultrn : 2 U.sonic : ON( 1)

Format :  
 Dist.base : Number Scaling : Auto Axis : LogX - LinearY

Data :  
 Median : 0.065µm SP.Area: 572520cm²/cm³ S.D. : 0.034µm  
 Mode : 0.081µm Mean : 0.073µm  
 C.V. : 46.66%

Span : (D 10.0-D 90.0) / D50 = 1.308

Dia. on %( 90.0%) :	0.121µm	% on Dia.( 0.400µm) :	100.0%
Dia. on %( 50.0%) :	0.065µm	% on Dia.( 0.300µm) :	100.0%
Dia. on %( 95.0%) :	0.137µm	% on Dia.( 0.200µm) :	99.8%
Dia. on %( 80.0%) :	0.101µm	% on Dia.( 0.100µm) :	79.3%
Dia. on %( 70.0%) :	0.087µm	% on Dia.( 1.000µm) :	100.0%



Size(µm)	Freq(%)	Und(%)	Size(µm)	Freq(%)	Und(%)	Size(µm)	Freq(%)	Und(%)
1019.5	0.00	100.00	26.11	0.00	100.00	0.669	0.00	100.00
890.1	0.00	100.00	22.80	0.00	100.00	0.584	0.00	100.00
777.1	0.00	100.00	19.90	0.00	100.00	0.510	0.00	100.00
678.5	0.00	100.00	17.38	0.00	100.00	0.445	0.00	100.00
592.4	0.00	100.00	15.17	0.00	100.00	0.389	0.01	100.00
517.2	0.00	100.00	13.25	0.00	100.00	0.339	0.01	99.99
451.6	0.00	100.00	11.56	0.00	100.00	0.296	0.02	99.98
394.2	0.00	100.00	10.10	0.00	100.00	0.259	0.03	99.96
344.2	0.00	100.00	8.816	0.00	100.00	0.226	0.13	99.93
300.5	0.00	100.00	7.697	0.00	100.00	0.197	0.50	99.81
262.4	0.00	100.00	6.720	0.00	100.00	0.172	1.62	99.31
229.1	0.00	100.00	5.867	0.00	100.00	0.150	3.81	97.69
200.0	0.00	100.00	5.122	0.00	100.00	0.131	6.25	93.88
174.6	0.00	100.00	4.472	0.00	100.00	0.115	8.37	87.64
152.5	0.00	100.00	3.905	0.00	100.00	0.100	9.23	79.26
133.1	0.00	100.00	3.409	0.00	100.00	0.087	9.51	70.04
116.2	0.00	100.00	2.976	0.00	100.00	0.076	9.43	60.52
101.5	0.00	100.00	2.599	0.00	100.00	0.067	9.14	51.09
88.58	0.00	100.00	2.269	0.00	100.00	0.058	8.78	41.95
77.34	0.00	100.00	1.981	0.00	100.00	0.051	8.45	33.17
67.52	0.00	100.00	1.729	0.00	100.00	0.044	8.61	24.73
58.95	0.00	100.00	1.510	0.00	100.00	0.039	8.08	16.11
51.47	0.00	100.00	1.318	0.00	100.00	0.034	8.05	8.05
44.94	0.00	100.00	1.151	0.00	100.00	0.029	0.00	0.00
39.23	0.00	100.00	1.005	0.00	100.00	0.026	0.00	0.00
34.25	0.00	100.00	0.877	0.00	100.00	0.022	0.00	0.00
29.91	0.00	100.00	0.766	0.00	100.00			